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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/059,521	01/29/2002	Ivan N. Rich	R103 1030.1	5794

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/059,521	RICH, IVAN N.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *29,30,32-41 and 45-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28,31 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-56* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/6 & 4/7 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group 1, claims 1-44, with traverse, filed 11/19/04 is acknowledged and has been entered. Claims 45-56 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Applicant's further election of the species in claim 31, drawn to erythropoietin, granulocyte-macrophage CSF, granulocyte CSF, stem cell factor, IL-3, IL-6, or Flt3L generating hematopoietic CF cell erythroid, and macrophage or megakaryocyte CFC-GEMM stem cells, is also acknowledged.

As applicant properly points out in the response to the restriction requirement set forth to Applicant on October 19, 2004, claims 29-44 have been inadvertently omitted from Group 1. Group I should properly include claims 1-44, claims 1-28 and 42-44 being generic, and claims 29-41 being the species claims, upon which the species in claim 31 has been elected for initial examination. Accordingly, claims 29, 30, and 32-41, directed to the species of cytokines used with the method, in addition to claims 45-56, are also withdrawn from further consideration since claims 29, 30, and 32-41 depend upon or otherwise include each of the limitations of the elected generic claim as required by 37 CFR 1.141.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is deemed proper and is therefore

made FINAL for reasons of record. Accordingly, claims 1-56 are pending. Claims 1-28, 31, and 42-44 are under examination.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the information regarding the date of filing of the instant application is incorrect. The date of filing of ASN 10/059,521 should be January 29, 2002, not January 29, 2001, and the date of filing of its provisional application, ASN 60/264,796 upon which the benefit of priority is being claimed, is January 29, 2001. Please correct.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 20, 23, 24, 42, 43, and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 in step a) is vague and indefinite because it is unclear how a "cell surface marker indicator" is capable of "selectively binding a cell surface marker". Specifically, while a ligand that is encompassed by the term "cell surface indicator"

which can bind a cell surface marker, it is unclear how it is capable of being selective, such as the selective binding capability of a monoclonal or polyclonal antibody.

Claim 42 is vague and indefinite because it is unclear as recited, what proliferative status of the primitive hematopoietic cells is suitable for transplantation and how it is identified.

Claim 43 has improper antecedent basis problem in reciting, "a population of primitive hematopoietic cells".

Claim 44 is vague and indefinite because it is unclear as recited, how the at least one test compound is identified, i.e. specific identity of the compound, by virtue of its ability to alter proliferation in comparison to a negative control. It does not appear to be compared to a known standard having specific activity towards proliferation of the target cell population, against which the test compound can be compared for activity and screened. At best, the method steps set forth in claim 44 appear to allow "identifying whether the test compound is capable of modulating the proliferative status of the plurality of target cell populations".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-28, 31, and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (Journal of Immunological Methods, 160: 81-88 (1993)) in view of Bell et al. (US 2002/0120098 A1).

Crouch et al. disclose an assay method for determining the proliferative status, i.e. cell proliferation, of a population of primitive hematopoietic cells. The hematopoietic cells are granulocyte-macrophage colony-forming cells (GM-CFC) and granulocyte colony-forming cells (G-CFC), i.e. TF-1 and NFS-60 cells, isolated from human peripheral blood, and are detected for cytokine dependent proliferation by stimulation of granulocyte-macrophage colony stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) (see Abstract). Initially, the hematopoietic cell lines are cultured and maintained in a cell growth culture medium containing 0% to 30% (12.5%) fetal bovine serum (fetal calf serum). Crouch et al. specifically contacts the cell population with luciferin-luciferase monitoring reagent which generates bioluminescence in the presence of adenosine triphosphate or ATP (see page 81, column 2 and page 82, columns 1 and 2). The amount of luminescence generated by the reagent indicates the amount of ATP in the cell population, wherein the amount of ATP indicates the proliferative status of the hematopoietic cells.

Crouch et al. differ from the instant invention in failing to disclose that the cell growth culture medium includes methyl cellulose having a concentration of about 0.4% to 0.7% methyl cellulose and maintained in an atmosphere having between about 3.5% to 7.5% oxygen. Crouch et al. further differ from the instant invention in failing to disclose generating a hematopoietic population enriched in progenitor cells and stem

cells from animal tissue such as bone marrow, fetal liver, and spleen, isolated from cow, sheep, pig, horse, goat, dog, cat, and primates, and determining their suitability for transplantation. Crouch et al. also does not teach isolating and identifying specific subpopulations of primitive hematopoietic cells using cell surface markers. Lastly, Crouch et al. does not teach contacting the primitive hematopoietic cells with a test compound and determining its ability to modulate proliferation of the cells.

Bell et al. disclose methods for enhancing stimulation of hematopoiesis (erythropoiesis) using hemoglobin. Hematopoiesis involves the proliferation of hematopoietic stem cells and hematopoietic progenitor cells and the stimulation is specific for hematopoietic colony-forming cell erythroid macrophage, megakaryocyte stem cells (CFC-GEMM) (see page 4, column 1, [0026], page 7, column 2, [0071], and page 9, column 2, [0085]). According to Bell et al., the burst forming unit-erythroid (BFU-E) represents the most primitive hematopoietic or erythroid progenitor and forms large multi-clustered hemoglobinized colonies (see page 1, column 1, [0004]). In practice, Bell et al. teach incubating primitive hematopoietic cells in a cell growth medium comprising 30% fetal bovine serum, about 0.4% to about 0.7% (0.8%) methyl cellulose which increases viscosity in culture media, and in an atmosphere having between about 3.5% to 7.5% (5%) oxygen. Bell et al. also teach contacting the sample with cytokine such as GM-CSF and Flt3 Ligand to generate a cell population substantially enriched in CFC-GEMM stem cells for use in cell proliferation assay (see page 7, column 2, [0071], page 9, column 2, [0084-0092], and Examples 1 and 2). Bell et al. disclose that erythroid progenitor colony formation is enhanced at lower, more

physiological oxygen tensions, such as 5% oxygen (see page 11, column 1, [0098-0101]. These enriched hematopoietic stem cells or progenitor cells can be obtained from bone marrow, cord blood, or peripheral blood, and if determined to have adequate proliferative status, can be transplanted into a recipient patient (see page 4, column 2, [0030] and page 7, column 2, [0078]). Hematopoietic stem cells or progenitor cells can also be obtained and enriched from animal tissue such as bone marrow, cord blood, fetal liver, or spleen, of dog, cow, horse, cat, pig, sheep, goat, chicken, primate, or human (see page 8, column 2, [0076-0078]). Bell et al. further teach that subpopulations of primitive hematopoietic cells are characterized by the presence of specific hematopoietic progenitor cell surface markers such as CD34 and glycophorin A (see page 12, column 1, [0105]). These subpopulations can be selectively isolated by binding the cells with antibodies specific for their cell surface markers such as anti-CD34 and anti-glycophorin A or by magnetic bead separation (STEMSEP^{TM} system) and selectively determined by flow cytometry or flow activated cell sorting (see page 17, column 1, [0044 and 0045] and Example 9). Bell et al. further teach contacting primitive hematopoietic cells having a target cell population with a test a compound (Ganciclovir) and determining its ability to modulate, i.e. inhibit, proliferation or differentiation of the target cell population. Result of the testing is compared with negative control (see Example 11).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Bell in using a culture growth medium having 30% fetal bovine serum, 0.8% methyl cellulose, and in an atmosphere having

between about 5% oxygen into the proliferation assay taught by Crouch because Bell specifically taught that hematopoietic progenitor cells or stem cells favor survival and growth in a medium having such composition for use in proliferation assays. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Bell into the proliferation assay of Crouch because methyl cellulose increases viscosity in culture media for proliferation of cells and Bell specifically taught that erythroid progenitor colony formation is even further enhanced at lower, more physiological oxygen tensions, i.e. 5% oxygen; hence, increasing the concentration of hematopoietic progenitor cells for use in a bioluminescence assay.

5. No claims are allowed.

Remarks

6. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Castello et al. (Experimental Hematology 23: 1367-1371 (1995)) teach assaying for proliferation of hematopoietic cells contained in culture medium having 0.8% methyl cellulose and 20% fetal bovine serum (see page 1368, column 1).

Moore (US Patent 5,328,844) discloses culture media for mammalian cells having fetal calf serum and methyl cellulose, both in different concentrations.

Alter (US Patent 5,580,724) discloses differential expansion of fetal stem cells in maternal circulation for use in prenatal genetic analysis. The fetal stem cells are

contained in culture media fetal calf serum and methyl cellulose, both in different concentrations.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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February 4, 2005